

# ANOGENITAL WARTS AND MOLLUSCUM CONTAGIOSUM

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Anogenital warts (condylomata acuminata, or venereal warts) represent the clinical expression of epidermal infection with the human papillomavirus (HPV) occurring on skin and mucosal surfaces of external genitalia and perianal areas. These lesions vary from harmless but disturbing papules to precursors of both benign and malignant neoplasias.

## **Etiology**

The HPV, member of the family Papovaviridae, is a nondeveloped virus with an icosahedral capsid containing a double-stranded, circular DNA genome. More than 60 different types of HPV have been recognized using DNA hybridization techniques under stringent condition. HPV 6 and, to a lesser degree, 11 are the most commonly isolated agents in genital warts; approximately 90% of condylomata acuminata contain one of these types. Less frequently isolated viral types from genital warts include 16, 18, 31, 33, and 35. Infection with more than one viral type has been estimated to occur in at least 8 to 14% cases.

The risk of malignant transformation in infections with HPV-6 and HPV-11, fortunately, appears to be low. By contrast, HPV types 16, 18, and 31, rarely identified in anogenital warts, are frequently associated with both carcinoma in situ and invasive carcinoma. Buschke-Lowenstein giant condylomata have been found to contain DNA of HPV 6, 11 and 16.

## **Epidemiology**

The incidence of anogenital warts has risen dramatically in the last 15 to 20 years. Both sexes are susceptible to infection. Although overt disease appears to be more common in men, the prevalence of infection may be higher in women. Prevalence is greatest between the ages of 17 and 33 years, with a peak incidence from ages 20 to 24 years. Venereal warts appear to be more common and widespread in patients with immunodeficiencies.

## **Transmission**

Genital warts are highly infective. They are commonly transmitted by sexual intercourse with infected partners. Two-thirds of persons who have sexual contact with partners who have condylomata acuminata will themselves develop lesions, but this may be an underestimate as the tiny warts on the penis and cervix may be overlooked or misdiagnosed.

The incubation period is 3-8 months, but is occasionally shorter (three weeks). Condyloma acuminatum in children is a potential indicator for sexual abuse. In new born, the suspected mode of transmission is passage through an infected birth canal. Older children may rarely become infected nonvenereally from caregivers either directly by manual contact or indirectly via fomites.

## **Clinical features**

Condyloma acuminatum typically presents as multiple or solitary penile, vulvar, vaginal, cervical, perineal, or perianal papules or plaques. The lesions may be skin-coloured, erythematous, or hyperpigmented. They often have a verrucous surface and may be lobulated. Lesions on the glans

penis and penile shaft may be filiform, and often pedunculated. Occasionally, papules may appear smooth, especially on the penile shaft. Some lesions, particularly in the perianal region, may assume large sizes and have a decidedly cauliflower-like appearance. On the vulva, genital warts are hyperplastic and may form large malodorous masses particularly in pregnancy, when they may be sufficiently massive to interfere with parturition.

In uncircumcised men, lesions commonly occur on the inner aspect of the foreskin, the fraenum and corona, whereas on the circumscribed penis lesions are found on the shaft and occasionally on the glans penis and at the urethral meatus. In the female venereal warts are found most frequently on posterior part of introitus, labia minora and clitoris, labia majora, perineum, anus, vagina, urethra, and cervix.

Macular and, to lesser extent, papular penile lesions have been associated with HPV types 16, 18, 31, 33, and 35, whereas acuminate morphology suggests infection with more innocuous types (HPV-6, HPV-11); however, the clinical appearance of anogenital lesions should not be taken to infer the type of HPV infection. External condylomata acuminata suggest the possibility of cervical or urethral infection.

Thus, evidence of HPV infection indicates the need for careful gynaecologic and urologic follow-up.

Genital warts may be widespread. In these cases they are often associated with an underlying immune defect as seen, for example, in AIDS.

The duration of genital warts varies from a few weeks to many years. Spontaneous regression may occur, more likely as a result of enhancement of cell-mediated immunity. During pregnancy warts grow at an accelerated pace and occasionally may obstruct the vagina necessitating surgical excision of the warts before term or even Caesarean section. After delivery warts usually involute. Complications of genital warts include itching and occasionally bleeding.

Secondary infection seems to be uncommon but may produce crusting or erythema, as may trauma. One particular rare type of wart is the giant condyloma of Buschke-Loewenstein which may develop in either sex. The giant condyloma develops in podophyllin-resistant warts of long duration, often in the phimotic preputial sac; it is progressively destructive and looks malignant; however, histologically it is benign and there are no metastasis.

## **Pathology**

In the nuclei of the superficial cells of genital warts virus particles are found. The cytological changes are characteristic, as seen in Papanicolaou-stained smears, and include enlargement of the squamous cells, multinucleation, hyperchromatosis, perinuclear clearing (koilocytosis) and dyskeratosis.

Histologically, genital warts present papillomatosis and considerable acanthosis. The most characteristic feature is the presence of areas in which large epithelial cells show hyperchromatic, round nucleus and perinuclear vacuolization. Because vacuolization is a normal occurrence in the upper portion of all mucosal surfaces, viral genesis is highly suspected only if cytoplasmic vacuolization extends into the deeper portions of the stratum malpighii. The dermis is usually edematous and moderately infiltrated with chronic inflammatory cells.

## **Malignant transformation**

HPV infection has been implicated in the development of carcinoma. Both squamous carcinoma and carcinoma in situ have been reported.

Clinically, the recent enlargement, aberration or induration of warts of relatively short duration, and the occurrence of pain and serosanguinous discharge, should arouse suspicion of malignant change. In any case in which neoplastic change is suspected, a biopsy is to be taken for histopathological examination.

### **Diagnosis and differential diagnosis**

The diagnosis of condyloma acuminatum is not always straightforward. Subclinical lesions can be revealed by whitening them with application of 2 to 5% acetic acid for 3-5 minutes on the genital skin. The sensitivity of this technique increases in proportion to the amount of time the acetic acid remains on the skin. However, because hyperplastic epithelium secondary to various factors other than HPV infection is identified by the acetic acid, the procedure is best employed by practitioners experienced in its performance and interpretation. Colposcopy may be invaluable in assessing vaginal and cervical lesions.

Condylomata lata of secondary syphilis are flat, disc-like, macerated lesions developing in the moist areas of the vulva and around the anus. Dark-field microscopy of scrapings taken from these lesions will invariably show the presence of numerous *Treponema pallidum* and the serology for syphilis is always strongly positive. *Molluscum contagiosum* should be differentiated clinically as it presents as small rounded papules with smooth surface, and an umbilicated centre. Other cutaneous proliferations to be differentiated from genital warts include pearly penile papules, fibroepitheliomas, seborrheic keratosis, neurofibromas and nevi. Hailey-Hailey disease and Darier's disease may also be misdiagnosed as condyloma acuminatum.

Bowenoid papulosis is a HPV-associated papular condition of the anogenital region that clinically resembles condyloma acuminatum, but histologically is consistent with carcinoma in situ; the lesions may progress to invasive carcinoma or regress spontaneously.

### **Treatment**

No treatment is really satisfactory. Accepted methods of treatment involve chemical and physical destruction or removal.

#### *Cytotoxic substances*

Podophyllin resin 5 to 10% in propylene glycol is effective in the treatment of genital warts unless they have formed vegetating masses or the so-called giant condyloma. Podophyllin is commonly painted onto lesions once or twice a week, with careful avoidance of the surrounding clinically normal skin that has to be protected with soft paraffin. Patients should be instructed to wash the treated area a few hours after the application, otherwise, a florid irritant dermatitis with erosion and ulceration may result. A solution 0.5% purified podophyllin is available for home application by the patient twice daily for 3 consecutive days of the week for up to 4 weeks. Podophyllin should not be used on the cervix and must not be used during pregnancy as it has mutagenic properties. After podophyllin application, there may be a severe local reaction, generally when the preparation is allowed to remain in contact too long. In such an event treatment is stopped and 1 per cent hydrocortisone ointment is applied twice daily until the reaction has cleared; podophyllin can then be reapplied with caution. Podophyllin, if used in excess, may give rise to systemic side effects, in particular peripheral neuropathy.

Trichloroacetic acid at various concentrations up to 80% is an alternative to podophyllin that pose fewer risks of local irritation and systemic toxicity. As with podophyllin, the acid is painted carefully onto the lesions, avoiding uninvolved skin; treatment may be repeated every 1 or 2 weeks until an adequate response is obtained. An advantage is that, unlike podophyllin, the treated area does not need to be cleansed after several hours, reducing concerns about patients for whom compliance is an issue. Unfortunately, the response is often incomplete and recurrences frequent. Five per cent fluorouracil cream or solution can be used for intrameatal warts.

### *Physical destructive methods*

Electrocautery is useful for all types of warts including common flat warts but has to be done under local anaesthesia. Cryotherapy, which is used without anaesthesia, is an excellent first-line therapy for condyloma acuminatum. When employed carefully, response rates are high and adverse sequelae are few.

Cryotherapy is also an acceptable treatment during pregnancy. It consists of a 10 to 15-second freeze with an open spray or a cotton-tipped applicator, perhaps repeated once after thawing. Because warts are treated separately this treatment can be time consuming; furthermore it is not practical for large warts. The most frequent adverse reactions include pain at the time of treatment, erosion and even ulceration. Patients with darkly pigmented skin may experience post-inflammatory hypopigmentation that may take months to improve.

The carbon dioxide laser has been employed for the destruction of recurrent or extensive condylomata acuminata. Laser therapy necessitate the use of local anesthesia and require expensive equipments. For extensive warts, especially at the perianal site, excision may be the only practical method.

### **Prognosis**

Many cases of condyloma acuminatum either fail to resolve with treatment or recur after apparent resolution. The refractory nature of condylomata acuminata may often be attributed to subclinical infection in the adjacent skin, failure to treat the involved skin adequately, or reinfection with the virus.

Possible reservoirs for reinfection or the existence of an immunosuppressive state should be sought.

### **Prevention**

The ideal management of condyloma acuminatum should involve primary prevention by identifying and educating those at risk. Sexual abstinence and monogamy are protective, whereas condoms may prevent transmission.

### **Molluscum contagiosum**

Molluscum contagiosum is a common, benign, viral disease of the skin and mucous membranes caused by a poxvirus (Molluscum contagiosum virus, MCV).

### **Etiology**

MCV is a poxvirus that is distinct morphologically, serologically and pathogenetically from other poxviruses. The virus is brick-shaped and measures 200 x 300 um. It has not been possible to grow

the virus and attempts at demonstrating antibodies in the serum have been disappointing. Two different MCV strains (I and II) have been identified. No clinical differences have been found between the two strains.

## Epidemiology

Although the disease may develop at any age, the vast majority of cases are found in children. MCV infection is believed to be transmitted by person-to-person spread by close bodily contacts and possibly by fomites. Genital lesions in adults are likely transmitted sexually. Patients with AIDS are at particular risk of MCV infection, with prevalence rates of 9 to 18 percent having been reported.

## Clinical manifestations

The incubation period is variously estimated at 14-50 days. The individual lesion is a smooth, pearly to flesh-coloured, dome-shaped papule. The lesion is often umbilicated, with a central pore through which a curd like core may be easily expressed (fig. 8, left). The lesions enlarge slowly reaching a diameter 5-10 mm in 6-12 weeks. Rarely, and usually when one or very few are present, a lesion may become as large as 3 or more cm in diameter.



Fig. 8 - Molluscum contagiosum.

Lesions may be located on any area of the skin and mucous membranes. They are usually grouped in one or two areas but may be widely disseminated, particularly in patients with AIDS.

Although lesions are usually asymptomatic, pruritus may be present, and an eczematous reaction may develop around some lesions. Patients with atopic dermatitis or with impaired immune function may develop secondary bacterial infections. The duration of the lesions is very variable and although most cases are self-limiting within 6-9 months, some persist for years.

## Pathology

The histologic appearance is characteristic. The epidermis grows down into the dermis as multiple, often closely packed lobules. Many of the epithelial cells in the lower epidermis contain large, intracytoplasmic inclusion bodies, the so-called "molluscum bodies". These inclusion bodies contain the viral particles and grow in size as they move toward the surface. In the centre of the lesion, the stratum corneum ultimately disintegrates, releasing the molluscum bodies and producing central crater forms.

## Diagnosis and Differential Diagnosis

The diagnosis of molluscum contagiosum is usually obvious by the distinctive clinical appearance of the lesions, stained smears of the expressed core and biopsy.

The solitary molluscum may resemble pyogenic granuloma, keratoacanthoma or an epithelioma and in some cases may be difficult to identify without histological examination. Multiple molluscum contagiosum must be differentiated from warts, varicella, pyoderma, papillomas, epitheliomas, and lichen planus. In patients with AIDS cutaneous cryptococcal infection may mimic the appearance of MCV infection.

## Treatment

Removal of lesions with a Volkman's spoon and touching the base with silver nitrate usually gives satisfactory results. Cryotherapy with liquid nitrogen may be an alternative effective treatment. More than one treatment is often necessary, because of recurrence or the development of new lesions. Thus, the patient should be re-examined at fortnightly intervals for 2-3 months after starting treatment. In patients with impaired immune function, molluscum contagiosum may be refractory to treatment.

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